

What is claimed is:

1. A modified IgG comprising a modified hinge region containing one or more amino acid modifications at a position corresponding to from position 233 to position 239 of human IgG1 relative to a corresponding wild-type hinge region and/or an amino acid modification at a residue corresponding to position 249 of a human IgG1 heavy chain, said modified IgG exhibiting reduced degradation of said modified IgG upon heating to 55°C for one week than a corresponding IgG not comprising said one or more amino acid modifications.
2. The modified IgG of claim 1 which is an IgG1.
3. The modified IgG of claim 1, wherein at least one of said one or more amino acid modifications is an amino acid substitution.
4. The modified IgG of claim 1 which is an IgG2, IgG3 or IgG4.
5. The modified IgG of claim 1 in which at least one of said one or more amino acid modifications is a substitution at a position corresponding to position 237 of a human gG1 heavy chain.
6. The modified IgG of claim 1 in which at least one of said one or more amino acid modifications is a substitution of a proline residue with a non-proline residue.
7. The modified IgG of claim 1 in which at least one of said one or more amino acid modifications is a substitution of a histidine, threonine, lysine or glutamic acid with a valine or isoleucine.
8. The modified IgG of claim 1 which is humanized.
9. The modified IgG of claim 1 which is human.
10. A method for increasing the stability of an IgG, said method comprising introducing one or more amino acid modifications in the hinge region of said IgG at a position corresponding to from position 233 to position 239 of human IgG1 and/or an amino acid modification at a residue corresponding to position 249 of a human IgG1 heavy chain, which one or more modifications result in reduced degradation of said IgG upon heating to 55°C for one week than a corresponding IgG not comprising said one or more amino acid modifications.

11. The method of claim 10 wherein said IgG is an IgG1.  
  
said human IgG1 heavy chain.
12. The method of claim 10, wherein at least one of said one or more amino acid modifications is an amino acid substitution.
13. The method of claim 10 in which said IgG is an IgG2, IgG3 or IgG4.
14. The method of claim 10 in which at least one of said one or more amino acid modifications is a substitution at a position corresponding to position 237 of said human IgG1 heavy chain.
15. The method of claim 10 in which at least one of said one or more amino acid modifications is a substitution of a proline residue with a non-proline residue.
16. The method of claim 10 in which at least one of said one or more amino acid modifications is a substitution of a histidine, threonine, lysine or glutamic acid with a valine or isoleucine.
17. The method of claim 10 in which said IgG is humanized.
18. The method of claim 10 in which said IgG is human.
19. A pharmaceutical composition comprising the modified IgG of any of claim 1 and a pharmaceutically acceptable carrier.
20. The pharmaceutical composition of claim 19 which is a liquid formulation.
21. The pharmaceutical composition of claim 20 which is formulated for parenteral, subcutaneous, intravenous, intramuscular, intranasal, or pulmonary delivery.
22. The pharmaceutical composition of claim 20 wherein said IgG is stable at ambient temperature for at least 1 year as determined by HPSEC.
23. The pharmaceutical composition of claim 20 wherein said IgG is stable at 40°C for at least 100 days as determined by HPSEC.
24. The pharmaceutical composition of claim 20 wherein said IgG is stable at 4°C for at least 3 years as determined by HPSEC.

25. The pharmaceutical composition of claim 20 wherein said IgG is stable at 4°C for 3-5 years as determined by HPSEC.

26. The pharmaceutical composition of claim 20 wherein said IgG is stable at 4°C for at least 5 years as determined by HPSEC.

27. A nucleic acid comprising a nucleotide sequence encoding the modified IgG of any of claim 1.

28. The nucleic acid of claim 27 which is isolated.

29. A vector comprising a nucleotide sequence encoding the modified IgG of any of claim 1.

30. A host cell comprising a nucleotide sequence encoding the modified IgG of any of claim 1 operably linked to a promoter.

31. The host cell of claim 30 which is a mammalian cell.

32. The host cell of claim 31 which is a myeloma cell.

33. A method of producing the modified IgG of any of claim 1, said method comprising culturing a host cell comprising a nucleotide sequence encoding said modified IgG under conditions appropriate for the expression of said IgG.

34. The method of claim 33 further comprising isolating said modified IgG.

35. The method of claim 34 wherein said host cell is a mammalian cell.

36. The method of claim 35 wherein said mammalian cell is a myeloma cell.

37. A method of screening a modified IgG for increased stability, said method comprising:

- (a) heating at 55°C for a week a modified IgG having one or more amino acid modifications in the hinge region of said IgG at a position corresponding to from position 233 to position 239 of human IgG1 and/or an amino acid modification at a position corresponding to position 249 of human IgG1;
- (b) fractionating the degradation products of the modified IgG from step (a) by size exclusion chromatography; and

- (c) analyzing fractions from step (b) containing said degradation products by mass spectrometry,

wherein the production of fewer degradation products by said modified IgG as compared to an IgG not having said one or more amino acid modifications indicates that said modified IgG has increased stability.

38. The method of claim 37 which comprises chemically or enzymatically modifying said modified IgG or said degradation products.

39. The method of claim 38 wherein said chemically or enzymatically modifying is by desalting, reduction, alkylation and/or deglycosylation.

40. The method of claim 38 wherein said degradation products are modified by deglycosylation.

41. The method of claim 40 wherein after said deglycosylation step, said degradation products are modified by reduction and alkylation.

42. The method of claim 41 wherein said mass spectrometry is by Matrix Assisted Laser Desorption Ionization-Time of Flight Mass Spectrometry (MALDI-TOF-MS) or Liquid Chromatography Electrospray Ionization Mass Spectrometry (LC-ESI-MS).